CLAIMS

1. An antibody characterized by its ability to bind to native human plasma hyaluronidase (hpHAse).

2. The antibody of claim 1, wherein the antibody binds to native hpHAse with a binding affinity K_a of 10^7 l/mole or more.

3. The antibody of claim 2, wherein the K_a is 10^8 l/mole or more.

4. An antibody that specifically binds to native human plasma hyaluronidase (hpHAse) produced by the process comprising the steps of:

(a) incubating a candidate antibody with a sample comprising native hpHAse, said incubating being for a time sufficient for formation of antibody-hpHAse complexes;

(b) contacting the sample with an insoluble support having anti-antibody and detectably-labeled hyaluronic acid bound thereto for a time sufficient for formation of anti-antibody-candidate antibody-hpHAse complexes; and

(c) exposing the sample in contact with the support to an acidic pH of about 3.4 to 3.7, thereby allowing hpHAse in the antibody-hpHAse complex to degrade the detectably labeled hyaluronic acid;

wherein samples associated with hyaluronic acid degradation comprise an anti-hpHAse antibody.

5. A hybridoma cell line 17E9 having ATCC accession number ATCC HB-12213.

6. A hybridoma cell line 4D5 having ATCC accession number ATCC HB-12214.

7. A method for screening candidate antibodies for binding to a native acid active hyaluronidase (aaHAse), the method comprising the steps of:

(a) incubating a candidate antibody with a sample comprising native aaHAse, said incubating being for a time sufficient for formation of antibody-aaHAse complexes;

(b) contacting the sample with an insoluble support having anti-antibody and detectably-labeled hyaluronic acid bound thereto for a time sufficient for formation of anti-antibody-candidate antibody-hpHAse complexes; and

(c) exposing the sample in contact with the support to an acidic pH of about 3.4 to 3.7, thereby allowing hpHAse in the antibody-aaHAse complex to degrade the detectably labeled hyaluronic acid;

wherein samples associated with hyaluronic acid degradation comprise an anti-aaHAse antibody.

8. The method of claim 7, wherein the acid active hyaluronidase is human plasma hyaluronidase.

9. A method of purifying human plasma hyaluronidase (hpHAse) from a sample, the method comprising;

contacting a sample comprising hpHAse with an anti-hpHAse antibody, said contacting being for a time sufficient for formation of anti-hpHase antibody-hpHAse complexes;

isolating hpHAse from the complexes.

10. The method of claim 9, wherein the sample is selected from the group consisting of blood, serum, plasma, and urine.

11. The method of claim 9, wherein hpHAse is recombinant.

12. A device for immunopurification of native human plasma hyaluronidase (hpHAse) comprising:

an insoluble support; and

an anti-hpHAse antibody characterized by an ability to bind hpHAse with a binding affinity of 10^7 l/mole or more.

13. The device of claim 12, wherein the antibody is characterized by an ability to bind 50% or more of hpHAse in a liquid flowable sample.

14. The device of claim 12, wherein a plurality of different antibodies are bound to the support surface and each antibody has a K_a of 10^7 l/mole or more relative to hpHAse.

15. An assay device for detection of hyaluronidase activity comprising:

an insoluble support;

biotinylated hyaluronic acid (bHA) covalently bound to the support.

16. The assay device of claim 15, wherein the biotinylated hyaluronic acid is formed in a one-step reaction of hyaluronic acid, 1-ethyl-dimethylaminopropyl carbodiamide (EDC), and biotin hydrazide.

17. The assay device of claim 15, wherein the bHA comprises at least one biotin moiety per every 100 disaccharide units in the hyaluronic acid moiety.

18. The assay device of claim 15, wherein the bHA is covalently bound to the support by at least one covalent bond per every 50 disaccharide units in the hyaluronic acid moiety.

19. A method for identifying a patient having or susceptible to a condition associated with a LuCa-1 defect, the method comprising the steps of:

contacting a sample from the patient with an anti-hpHAse antibody, the sample being selected from the group consisting of tissue, blood, plasma, serum, and urine, said contacting being for a time sufficient for formation of anti-hpHAse antibody-hpHAse complexes;

detecting the amount of hpHAse present in the sample; and

comparing the amount of hpHAse detected in the sample with an amount of hpHAse in a control sample containing a known amount of hpHAse correlated with a normal level of hpHAse;

wherein detection of an amount of hpHAse in the patient sample that is less than the amount of hpHAse in the control sample is indicative of a LuCa-1 defect in the patient.

20. Substantially purified human plasma hyaluronidase characterized by a fatty acid moiety that is resistant to cleavage by phospholipase C, phospholipase D, and N-glycosidase-F.

21. A method of purifying a native acid active hyaluronidase (aaHAse) from a sample, the method comprising the steps of:

(a) dissolving a sample suspected of containing an aaHAse in a solution at a temperature substantially less than room temperature, the solution comprising a non-ionic detergent;

(b) raising the temperature of the solution to a temperature substantially greater than room temperature, said raising resulting in the formation of a detergent-rich phase comprising aaHAse and a detergent-poor phase; and

(c) isolating aaHAse from the detergent-rich phase.

22. The method of claim 21, wherein the aaHAse is hpHAse and steps (a)-(c) are repeated twice.

23. The method of claim 21, wherein the sample is selected from the group consisting of blood, serum, plasma, and urine.

24. An expression system for production of recombinant hpHAse, the system comprising a transformed cell containing a nucleic acid construct comprising hpHAse-encoding nucleic acid operably linked to a eukaryotic promoter.

25. The expression system of claim 24, wherein the transformed cell is an HEK cell.

26. A formulation for administration of human plasma hyaluronidase (hpHAse) to a patient having a condition associated with a LuCa-1 gene defect comprising:

a) a therapeutically effective amount of a substantially pure human plasma hyaluronidase polypeptide; and

b) a pharmaceutically acceptable carrier.

27. The formulation of claim 26, wherein the carrier is a liposome.

28. A method of treating a patient having or susceptible to cancer associated with a LuCa-1 defect, the method comprising administering to the patient a human plasma hyaluronidase polypeptide in an amount effective to suppress tumor growth.

29. The method of claim 28, wherein said administering is by peritumoral injection.

30. The method of claim 28, wherein the cancer is a metastatic carcinoma.

31. A method of treating a patient having or susceptible to cancer associated with a defective LuCa-1 gene, the method comprising:

introducing into a cell of a patient having a LuCa-1 defect a construct comprising a nucleotide sequence encoding a human plasma hyaluronidase polypeptide and a eukaryotic promoting sequence operably linked thereto, said introducing resulting in the genetic transformation of the cell so that the nucleotide sequence expresses human plasma hyaluronidase

32. An isolated recombinant human plasma hyaluronidase polypeptide.

33. A method of making a recombinat human plasma hylauronidase polypeptide, the method comprising the steps of:

introducing into a host cell a nucleotide sequence encoding a human plasma hylaruonidase polypeptide;

culturing the host cell so as to allow for expression of the polypeptide from the introduced sequence; and

isolating human plasma hylauronidase polypeptide.